

What is claimed is:

1. A compound of Formula (I):



or a pharmaceutically acceptable salt form thereof, wherein;

E^{CP} is an enzyme cleavable peptide conjugated to A and selected from:

10

Cap- Paa -Xa2 -Gly - Xp1 - Laa -;

Cap- Xa2 - Gly - Xp1 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Gly - Xp1 - Xp2 - Laa -;

15

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

20

Cap- Paa - Xa2 - Sar - Xp1 - Laa -;

Cap- Xa2 - Sar - Xp1 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Sar - Xp1 - Xp2 - Laa -;

25

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -; and

Cap- Sar - Xp1 - Xp2 - Xp3 - Laa -;

30

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Rph, Npa, Tzc, or proline mimetic;

Xa2 is an amino acid;

Xp1 is an amino acid wherein -Gly-Xp1- or -Sar-Xp1- form a bond cleavable by
a matrixin;

Xp2 is an amino acid;

Xp3 is an amino acid;

Laa is an amino acid selected from Leu, Ile, Nle, β -homo-Leu, Hol, Hos, Ala, α -Ala, Cha, Cba, Cta, 4-pyridyl-Ala, 3-pyridyl-Ala, 2-pyridyl-Ala, Gly, Abu, Aib, Iva, Nva, Ahx, Aph, Amh, Phe, Bip, Glu, Arg, Trp, Tyr, O-(C₁-C₄ alkyl)-Tyr, O-(phenyl(C₁-C₄ alkyl)-)-Tyr, (C₃-C₈ alkyl)-Gly, and aminoalkyl carboxylic acid;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid;

R is an amino capping group;

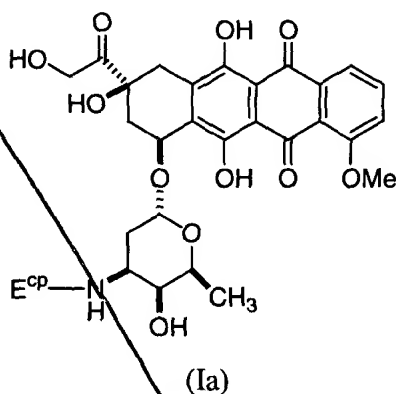
and

A is an antineoplastic agent.

2. A compound of Claim 1 wherein A is doxorubicin, a doxorubicin derivative, or a doxorubicin analogue.

3. A compound of Claim 2 wherein A is doxorubicin.

4. A compound of Claim 3 of Formula (Ia):



or a pharmaceutically acceptable salt form thereof, wherein;

ECP is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa -;

5

Cap- Xa2 - Gly - Xp1 - Laa -;
 Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;
 Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;
 Cap- Gly - Xp1 - Xp2 - Laa -;
 Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;
 Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;
 Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

10

Cap- Paa - Xa2 - Sar - Xp1 - Laa -;
 Cap- Xa2 - Sar - Xp1 - Laa -;
 Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Laa -;
 Cap- Xa2 - Sar - Xp1 - Xp2 - Laa -;
 Cap- Sar - Xp1 - Xp2 - Laa -;
 Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -;
 Cap- Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -; and
 Cap- Sar - Xp1 - Xp2 - Xp3 - Laa -;

15

20

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic;
 Xa2 is an amino acid;
 Xp1 is an amino acid wherein -Gly-Xp1- or -Sar-Xp1- form a bond cleavable by
 a matrixin;
 Xp2 is an amino acid;
 Xp3 is an amino acid;

25

Laa is an amino acid selected from Leu, Ile, Nle, β -homo-Leu, Hol, Hos, Ala, α -
 Ala, Cha, Cba, Cta, 4-pyridyl-Ala, 3-pyridyl-Ala, 2-pyridyl-Ala,
 Gly, Abu, Aib, Iva, Nva, Ahx, Aph, Amh, Phe, Bip, Glu, Arg, Trp, Tyr,
 O-(C₁-C₄ alkyl)-Tyr, O-(phenyl(C₁-C₄ alkyl))-Tyr, (C₃-C₈ alkyl)-Gly,
 and aminoalkyl carboxylic acid;

30

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;
 Xa4- is an amino acid;

R is selected from: $\text{H}_3\text{CC}(=\text{O})-$;

$\text{HOC}(=\text{O})-(\text{CH}_2)_v\text{C}(=\text{O})-$,

wherein v is 1, 2, 3, 4, 5, or 6;

$\text{H}_3\text{CO}-(\text{CH}_2\text{CH}_2\text{O})_t-\text{CH}_2\text{C}(=\text{O})-$,

5 $\text{HO}_2\text{CCH}_2\text{O}-(\text{CH}_2\text{CH}_2\text{O})_t-\text{CH}_2\text{C}(=\text{O})-$,

$\text{H}_2\text{N}-(\text{CH}_2\text{CH}_2\text{O})_t-\text{CH}_2\text{C}(=\text{O})-$, and

$\text{H}_3\text{CC}(=\text{O})\text{HN}-(\text{CH}_2\text{CH}_2\text{O})_t-\text{CH}_2\text{C}(=\text{O})-$,

wherein t is 1, 2, 3, or 4;

$\text{R}^1-\text{C}(=\text{O})-$;

10 $\text{R}^1-\text{S}(=\text{O})_2-$;

$\text{R}^1-\text{NHC}(=\text{O})-$;

$\text{R}^{1a}-\text{CH}_2\text{C}(=\text{O})-$;

proline substituted with $-\text{OR}^3$;

C_1-C_4 alkyl substituted with 0-1 R^4 ;

15 2-carboxyphenyl- $\text{C}(=\text{O})-$; and

$-(\text{O}=\text{C})\text{-phenyl}-\text{C}(=\text{O})-$;

R^1 is C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from

$-\text{OH}$, methoxy and $-\text{CO}_2\text{H}$;

20 5-6 membered heterocycle; said heterocycle being saturated, partially

saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4

heteroatoms selected from N, O, and S; said heterocycle optionally

substituted with 1 or 2 $-\text{OH}$, methoxy or $-\text{CO}_2\text{H}$;

phenyl substituted with 0, 1, or 2 substituents selected from $-\text{OH}$,

25 methoxy and $-\text{CO}_2\text{H}$, or

C_1-C_6 alkyl substituted with 0-4 R^{1a} ;

R^{1a} is $-\text{OH}$, C_1-C_3 alkyl, C_1-C_4 alkoxy, $-\text{CO}_2\text{H}$, $-\text{N}(\text{CH}_2\text{CH}_2)_2\text{N}-\text{R}^2$, $-\text{SO}_3\text{H}$;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from

methoxy and $-\text{OH}$;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH;

phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

R² is -H, H₂N(C₂-C₄ alkyl)-, acetyl(H)N(C₂-C₄ alkyl)-, or acetyl;

R³ is -H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, phenyl, or benzyl;

R⁴ is -OH, C₁-C₃ alkyl, C₁-C₄ alkoxy, -CO₂H, -N(CH₂CH₂)₂N-R² ;

C₃-C₆ cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

C₆-C₁₀ carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.

5. A compound of Claim 4 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein:

E^{CP} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa - ;
Cap- Xa2 - Gly - Xp1 - Laa - ;
Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa - ;
Cap- Xa2 - Gly - Xp1 - Xp2 - Laa - ;
Cap- Gly - Xp1 - Xp2 - Laa - ;
Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa - ;
Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa - ;
Cap- Gly - Xp1 - Xp2 - Xp3 - Laa - ;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic;

Xa2 is an amino acid;

Xp1 is an amino acid wherein -Gly-Xp1- forms a bond cleavable by a matrixin;

Xp2 is an amino acid;

Xp3 is an amino acid;

5 Laa is an amino acid selected from Leu, Ile, Nle, β -homo-Leu, Hol, Hos, Ala, β -Ala, Cha, Cba, Cta, 4-pyridyl-Ala, Abu, Aib, Iva, Nva, Phe, Bip, Tyr, O-benzyl-Tyr; and

10 Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid;

R is selected from: $\text{H}_3\text{CC}(=\text{O})-$;

$\text{HOC}(=\text{O})-(\text{CH}_2)_v\text{C}(=\text{O})-$,

wherein v is 1, 2, 3, or 4;

15 $\text{H}_3\text{CO}-(\text{CH}_2\text{CH}_2\text{O})_t\text{CH}_2\text{C}(=\text{O})-$,

$\text{HO}_2\text{CCH}_2\text{O}-(\text{CH}_2\text{CH}_2\text{O})_t\text{CH}_2\text{C}(=\text{O})-$,

$\text{H}_2\text{N}-(\text{CH}_2\text{CH}_2\text{O})_t\text{CH}_2\text{C}(=\text{O})-$, and

$\text{H}_3\text{CC}(=\text{O})\text{HN}-(\text{CH}_2\text{CH}_2\text{O})_t\text{CH}_2\text{C}(=\text{O})-$,

wherein t is 1, 2, or 3;

20 $\text{R}^1\text{-C}(=\text{O})-$;

$\text{R}^1\text{-S}(=\text{O})_2-$;

$\text{R}^1\text{-NHC}(=\text{O})-$;

$\text{R}^1\text{-CH}_2\text{C}(=\text{O})-$;

proline substituted with $-\text{OR}^3$;

25 $\text{C}_1\text{-C}_4$ alkyl substituted with 0-1 R^4 ;

$\text{HO}_3\text{SCH}_2\text{CH}(\text{NH}_2)\text{C}(=\text{O})-$;

2-carboxyphenyl- $\text{C}(=\text{O})-$; and

$-(\text{O}=\text{C})\text{-phenyl-C}(=\text{O})-$;

30 R^1 is $\text{C}_3\text{-C}_6$ cycloalkyl substituted with 0, 1, or 2 substituents selected from

Sub
a2
cont

-OH, methoxy and -CO₂H;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH, methoxy or -CO₂H;

phenyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and -CO₂H; or

C₁-C₆ alkyl substituted with 0-4 R^{1a};

R^{1a} is -OH, C₁-C₃ alkyl, C₁-C₄ alkoxy, -CO₂H, -N(CH₂CH₂)₂N-R², -SO₃H;

C₃-C₆ cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH;

phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

R² is -H, H₂N(C₂-C₄ alkyl)-, acetyl(H)N(C₂-C₄ alkyl)-, or acetyl;

R³ is -H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, phenyl, or benzyl;

R⁴ is -OH, C₁-C₃ alkyl, C₁-C₄ alkoxy, -CO₂H, -N(CH₂CH₂)₂N-R²;

C₃-C₆ cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

C₆-C₁₀ carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.

6. The compound of Claim 5, wherein -Gly-Xp1- forms a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.
7. The compound of Claim 5, wherein -Gly-Xp1- forms a bond cleavable by the matrixin selected from MMP-2 and MMP-9.
8. The compound of Claim 5, wherein -Gly-Xp1- forms a bond cleavable by the matrixin MMP-14.
9. The compound of Claim 5, wherein -Gly-Xp1- forms a bond cleavable by MMP-2, MMP-9, and MMP-14.

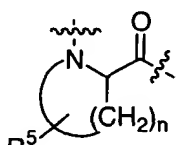
10. A compound of Claim 5 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

ECP is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa -;
 Cap- Xa2 - Gly - Xp1 - Laa -;
 Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;
 Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;
 Cap- Gly - Xp1 - Xp2 - Laa -;
 Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;
 Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;
 Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

wherein -Gly-Xp1- forms a bond cleavable by a matrixin;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic of

formula: ; wherein R⁵ is selected from H, halogen, C₁-C₆ alkyl, -OH, C₁-C₆ alkoxy, and benzyloxy; and n is 2, 3, 4, or 5;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β -Ala, γ -Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Cya, Hca, and Spa;

Xp1 is an amino acid selected from Hof; Leu; Bip; Phe; nor-Leu; Tha; Phg; Val; Glu; Asn; Ser; Ala; homo-Tyr; Aze; 4-aza-Hof; O-(3-pyridyl)-Tyr; O-(4-pyridyl)-Tyr; O-benzyl-Tyr; O-benzyl-Thr; O-benzyl-Ser; O-methyl-Ser; O-allyl-Ser; 4-nitro-Hof; N-methyl-Leu; O-(4-pyridylmethyl)-Tyr; 4-hydroxy-phenyl-Gly; phenylpropyl-Gly; styryl-Ala, or 2Nal;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu; His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-Dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, Cya, Hca, Spa, morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Xp3 is an amino acid selected from Tyr, Ala, Ser, Leu, Hof, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, and Val;

Laa is an amino acid selected from Leu, Ile, Nle, β -homo-Leu, Hol, Hos, Ala, β -Ala, Cha, Cba, Cta, 4-pyridyl-Ala, Abu, Aib, Iva, Nva, and Phe;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ -Glu, Dmg, Ala, Arg, Asn, Asp, β -Asp, Aze, Cha, Cys, Dpa, Gln, Glu, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Sar, Ser, Thr, Trp, Tyr, or Val;

R is selected from: $\text{H}_3\text{CC}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

5 $\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{HO}_2\text{CCH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_2\text{NCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

10 $\text{H}_2\text{NCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_3\text{CC}(=\text{O})\text{HNCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_3\text{CC}(=\text{O})\text{HNCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_2\text{NCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{CC}(=\text{O})\text{HNCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{C}(=\text{O})-$;

15 $\text{H}_3\text{CC}(=\text{O})\text{N}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{C}(=\text{O})-$;

$\text{O}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{NHC}(=\text{O})-$

$\text{HO}_2\text{CCH}_2\text{C}(\text{CO}_2\text{H})(\text{OH})\text{CH}_2\text{C}(=\text{O})-$,

$\text{HO}_2\text{CCH}_2\text{C}(\text{CH}_3)(\text{OH})\text{CH}_2\text{C}(=\text{O})-$,

2-carboxycyclohexyl- $\text{C}(=\text{O})-$;

20 2-carboxycyclopentyl- $\text{C}(=\text{O})-$;

carbobenzyloxy;

4-methoxy-benzenesulfonyl;

cyclopropylcarbonyl;

cyclobutylcarbonyl;

25 3-pyridinecarbonyl;

2-pyrazinecarbonyl;

tetrazoleacetyl;

pivaloyl;

methoxyacetyl;

30 hydroxyproline; and

4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

11. The compound of Claim 10, wherein -Gly-Xp1- forms a bond cleavable by the matrixin selected from MMP-2 , MMP-9, and MMP-14.

5 12. The compound of Claim 10, wherein -Gly-Xp1- forms a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

13. The compound of Claim 10, wherein -Gly-Xp1- forms a bond cleavable by the matrixin MMP-14.

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14. The compound of Claim 10, wherein -Gly-Xp1- forms a bond cleavable by MMP-2 , MMP-9, and MMP-14.

15. A compound of Claim 10 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

ECP is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Leu - Laa -;

Cap- Paa - Xa2 - Gly - Hof - Laa -;

Cap- Xa2 - Gly - Leu - Laa -;

Cap- Xa2 - Gly - Hof - Laa -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Laa -;

Cap- Xa2 - Gly - Leu- Xp2 - Laa -;

Cap- Xa2 - Gly - Hof - Xp2 - Laa -;

Cap- Gly - Leu - Xp2 - Laa -; and

Cap- Gly - Hof - Xp2 - Laa -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

30 Paa is a Pro, Hyp, Aze, homo-Pro, or Npa;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β -Ala, γ -Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Cya, Hca, and Spa;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu; His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-Dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, Cya, Hca, Spa, morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Laa is an amino acid selected from Leu, Cha, Nle, and Hol;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ -Glu, and Dmg;

R is selected from: $\text{H}_3\text{CC}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{HO}_2\text{CCH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_2\text{NCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_2\text{NCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_3\text{CC}(=\text{O})\text{HNCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_3\text{CC}(=\text{O})\text{HNCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$,

$\text{H}_2\text{NCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{CC}(=\text{O})\text{HNCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{CC}(=\text{O})\text{N}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{C}(=\text{O})-$;

$\text{O}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{NHC}(=\text{O})-$

$\text{HO}_2\text{CCH}_2\text{C}(\text{CO}_2\text{H})(\text{OH})\text{CH}_2\text{C}(=\text{O})-$,
 $\text{HO}_2\text{CCH}_2\text{C}(\text{CH}_3)(\text{OH})\text{CH}_2\text{C}(=\text{O})-$,
 2-carboxycyclohexyl-C(=O)-;
 2-carboxycyclopentyl-C(=O)-;
 5 carbobenzyloxy;
 4-methoxy-benzenesulfonyl;
 cyclopropylcarbonyl;
 cyclobutylcarbonyl;
 3-pyridinecarbonyl;
 10 2-pyrazinecarbonyl;
 tetrazoleacetyl;
 pivaloyl;
 methoxyacetyl;
 hydroxyproline; and
 15 4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

16. The compound of Claim 15, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.

20 17. The compound of Claim 15, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

18. The compound of Claim 15, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin MMP-14.

25

19. The compound of Claim 15, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by MMP-2, MMP-9, and MMP-14.

20. A compound of Claim 15 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{CP} is an enzyme cleavable peptide selected from:

Cap-Paa - Xa2 - Gly - Leu - Leu -;

5

Cap- Paa - Xa2 - Gly - Leu - Cha -;

Cap- Paa - Xa2 - Gly - Leu - Nle -;

Cap- Paa - Xa2 - Gly - Leu - Hol -;

Cap- Paa - Xa2 - Gly - Hof - Leu -;

Cap- Paa - Xa2 - Gly - Hof - Cha -;

Cap- Paa - Xa2 - Gly - Hof - Nle -;

Cap- Paa - Xa2 - Gly - Hof - Hol -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Leu -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Cha -;

10

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Nle -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Hol -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Leu -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Cha -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Nle -;

15

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Hol -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

Paa is a Pro, Hyp, Aze, homo-Pro, or Npa;

20

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β -Ala, γ -Abu, Cha,

Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-

Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof,

25

Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro),

Pro, Sar, Ser, Thr, Trp, and Tyr;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu; His;

Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-Dimethyl-

30

Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe,

Phe(4-fluoro), Pro, Sar, Thr, Trp; morpholinylpropyl-Gly; O-(4-

pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ -Glu, and Dmg;

5

R is selected from: $\text{H}_3\text{CC}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$;

2-carboxycyclohexyl- $\text{C}(=\text{O})-$;

2-carboxycyclopentyl- $\text{C}(=\text{O})-$; and

tetrazoleacetyl.

15 21. The compound of Claim 20, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.

22. The compound of Claim 20, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

20

23. The compound of Claim 20, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin MMP-14.

25

24. The compound of Claim 20, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by MMP-2, MMP-9, and MMP-14.

30

25. A compound of Claim 15 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{CP} is an enzyme cleavable peptide selected from:

Cap- Xa2 - Gly - Leu - Leu -;

Cap- Xa2 - Gly - Leu - Cha -;

Cap- Xa2 - Gly - Leu - Nle -;

Cap- Xa2 - Gly - Leu - Hol -;

Cap- Xa2 - Gly - Hof - Leu -;

Cap- Xa2 - Gly - Hof - Cha -;

Cap- Xa2 - Gly - Hof - Nle -;

Cap- Xa2 - Gly - Hof - Hol -;

Cap- Xa2 - Gly - Leu - Xp2 - Leu -;

Cap- Xa2 - Gly - Leu - Xp2 - Cha -;

Cap- Xa2 - Gly - Leu - Xp2 - Nle -;

Cap- Xa2 - Gly - Leu - Xp2 - Hol -;

Cap- Xa2 - Gly - Hof - Xp2 - Leu -;

Cap- Xa2 - Gly - Hof - Xp2 - Cha -;

Cap- Xa2 - Gly - Hof - Xp2 - Nle -; and

Cap- Xa2 - Gly - Hof - Xp2 - Hol -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β -Ala, γ -Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, and Tyr;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu; His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-Dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp; morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ -Glu, and Dmg;

R is selected from: $\text{H}_3\text{CC}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

5 $\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$;

$\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})-$;

2-carboxycyclohexyl- $\text{C}(=\text{O})-$;

2-carboxycyclopentyl- $\text{C}(=\text{O})-$; and

10 tetrazoleacetyl.

26. The compound of Claim 25, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2, MMP-9, and MMP-14.

15 27. The compound of Claim 25, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin selected from MMP-2 and MMP-9.

28. The compound of Claim 25, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by the matrixin MMP-14.

20 29. The compound of Claim 25, wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by MMP-2, MMP-9, and MMP-14.

30. A compound of Claim 4 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

ECP is an enzyme cleavable peptide selected from:

SEQ. ID. NO: 185: R- γ -E -P-Orn-G-Hof-E-L-;

SEQ. ID. NO: 186: R- γ -E -P-L-G-(O-benzyl-S)-Y-L-;

SEQ. ID. NO: 187: R- γ -E -P-L-G-(O-benzyl-S)-Y-Nle-;

SEQ. ID. NO: 188: R -P-L-G-(O-benzyl-S)-Y-L-;

SEQ. ID. NO: 189: R -P-L-G-(O-methyl-S)-Y-L-;

SEQ. ID. NO: 190: R -P-L-G-(azaHof)-Y-L-;
 SEQ. ID. NO: 191: R -P-L-G-Hof-Y-L-;
 SEQ. ID. NO: 192: R -P-L-G-Hof-E-L-;
 SEQ. ID. NO: 193: R -P-L-G-(O-benzyl-S)-Y-Nle-;
 SEQ. ID. NO: 194: R -P-L-G-(O-methyl-S)-Y-Nle-;
 SEQ. ID. NO: 195: R -P-L-G-(azaHof)-Y-Nle-;
 SEQ. ID. NO: 196: R -P-L-G-Hof-Y-Nle-;
 SEQ. ID. NO: 197: R -P-L-G-Hof-E-Nle-;
 SEQ. ID. NO: 198: R -P-L-G-(O-benzyl-S)-Y-Hol-;
 SEQ. ID. NO: 199: R -P-L-G-(O-methyl-S)-Y-Hol-;
 SEQ. ID. NO: 200: R -P-L-G-(azaHof)-Y-Hol-;
 SEQ. ID. NO: 201: R -P-L-G-Hof-Y-Hol-;
 and
 SEQ. ID. NO: 202: R -P-L-G-Hof-E-Hol-;

R is selected from: $\text{H}_3\text{CC}(=\text{O})-$;

$\text{HOC}(=\text{O})-(\text{CH}_2)_v\text{C}(=\text{O})-$,

wherein v is 1, 2, 3, 4, 5, or 6;

$\text{H}_3\text{CO}-(\text{CH}_2\text{CH}_2\text{O})_t\text{CH}_2\text{C}(=\text{O})-$,

$\text{HO}_2\text{CCH}_2\text{O}-(\text{CH}_2\text{CH}_2\text{O})_t\text{CH}_2\text{C}(=\text{O})-$,

$\text{H}_2\text{N}-(\text{CH}_2\text{CH}_2\text{O})_t\text{CH}_2\text{C}(=\text{O})-$, and

$\text{H}_3\text{CC}(=\text{O})\text{HN}-(\text{CH}_2\text{CH}_2\text{O})_t\text{CH}_2\text{C}(=\text{O})-$,

wherein t is 1, 2, 3, or 4;

$\text{R}^1\text{-C}(=\text{O})-$;

$\text{R}^1\text{-S}(=\text{O})_2-$;

$\text{R}^1\text{-NHC}(=\text{O})-$;

$\text{R}^1\text{a-CH}_2\text{C}(=\text{O})-$;

proline substituted with $-\text{OR}^3$;

$\text{C}_1\text{-C}_4$ alkyl substituted with 0-1 R^4 ;

2-carboxyphenyl- $\text{C}(=\text{O})-$; and

~~-(O=)C-phenyl-C(=O)-;~~

~~R¹ is C₃-C₆ cycloalkyl substituted with 0, 1, or 2 substituents selected from~~

~~-OH, methoxy and -CO₂H;~~

5

~~5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH, methoxy or -CO₂H;~~

10

~~phenyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and -CO₂H; or~~

~~C₁-C₆ alkyl substituted with 0-4 R^{1a};~~

~~R^{1a} is -OH, C₁-C₃ alkyl, C₁-C₄ alkoxy, -CO₂H, -N(CH₂CH₂)₂N-R², -SO₃H;~~

~~C₃-C₆ cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;~~

15

~~5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH;~~

~~phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;~~

~~R² is -H, H₂N(C₂-C₄ alkyl)-, acetyl(H)N(C₂-C₄ alkyl)-, or acetyl;~~

~~R³ is -H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, phenyl, or benzyl;~~

~~R⁴ is -OH, C₁-C₃ alkyl, C₁-C₄ alkoxy, -CO₂H, -N(CH₂CH₂)₂N-R²;~~

~~C₃-C₆ cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;~~

25

~~5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or~~

~~C₆-C₁₀ carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.~~

31. A compound of Claim 30 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

E^{CP} is an enzyme cleavable peptide selected from:

SEQ. ID. NO: 185: R-γ-E -P-Orn-G-Hof-E-L-;
SEQ. ID. NO: 186: R-γ-E -P-L-G-(O-benzyl-S)-Y-L-;
SEQ. ID. NO: 187: R -γ-E -P-L-G-(O-benzyl-S)-Y-Nle-;
SEQ. ID. NO: 188: R -P-L-G-(O-benzyl-S)-Y-L-;
SEQ. ID. NO: 189: R -P-L-G-(O-methyl-S)-Y-L-;
SEQ. ID. NO: 190: R -P-L-G-(azaHof)-Y-L-;
SEQ. ID. NO: 191: R -P-L-G-Hof-Y-L-;
SEQ. ID. NO: 192: R -P-L-G-Hof-E-L-;
SEQ. ID. NO: 193: R -P-L-G-(O-benzyl-S)-Y-Nle-;
SEQ. ID. NO: 194: R -P-L-G-(O-methyl-S)-Y- Nle -;
SEQ. ID. NO: 195: R -P-L-G-(azaHof)-Y- Nle -;
SEQ. ID. NO: 196: R -P-L-G-Hof-Y- Nle -;
SEQ. ID. NO: 197: R -P-L-G-Hof-E- Nle -;
SEQ. ID. NO: 198: R -P-L-G-(O-benzyl-S)-Y-Hol-;
SEQ. ID. NO: 199: R -P-L-G-(O-methyl-S)-Y- Hol -;
SEQ. ID. NO: 200: R -P-L-G-(azaHof)-Y- Hol -;
SEQ. ID. NO: 201: R -P-L-G-Hof-Y- Hol -;
and
SEQ. ID. NO: 202: R -P-L-G-Hof-E- Hol -;

R is selected from: H₃CC(=O)-;

HOC(=O)CH₂CH₂C(=O)-;

HOC(=O)CH₂CH₂CH₂C(=O)-;

HOC(=O)CH₂CH₂CH₂CH₂C(=O)-;

H₃COCH₂CH₂OCH₂C(=O)-;

5 $\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C(=O)-}$,
 $\text{HO}_2\text{CCH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C(=O)-}$,
 $\text{H}_2\text{NCH}_2\text{CH}_2\text{OCH}_2\text{C(=O)-}$,
 $\text{H}_2\text{NCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C(=O)-}$,
 $\text{H}_3\text{CC(=O)HNCH}_2\text{CH}_2\text{OCH}_2\text{C(=O)-}$,
 $\text{H}_3\text{CC(=O)HNCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C(=O)-}$,
 $\text{H}_2\text{NCH}_2\text{CH}_2\text{N(CH}_2\text{CH}_2)_2\text{NCH}_2\text{C(O)-}$;
 $\text{H}_3\text{CC(=O)HNCH}_2\text{CH}_2\text{N(CH}_2\text{CH}_2)_2\text{NCH}_2\text{C(O)-}$;
 $\text{H}_3\text{CC(=O)N(CH}_2\text{CH}_2)_2\text{NCH}_2\text{C(O)-}$;
 10 $\text{O(CH}_2\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{NHC(O)-}$
 $\text{HO}_2\text{CCH}_2\text{C(CO}_2\text{H)(OH)CH}_2\text{C(=O)-}$,
 $\text{HO}_2\text{CCH}_2\text{C(CH}_3)_2\text{(OH)CH}_2\text{C(=O)-}$,
 15 2-carboxycyclohexyl-C(=O)-;
 2-carboxycyclopentyl-C(=O)-;
 carbobenzyloxy;
 4-methoxy-benzenesulfonyl;
 cyclopropylcarbonyl;
 cyclobutylcarbonyl;
 3-pyridinecarbonyl;
 2-pyrazinecarbonyl;
 20 tetrazoleacetyl;
 pivaloyl;
 methoxyacetyl;
 hydroxyproline; and
 25 4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

32. A compound of Claim 30 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

E^{CP} is an enzyme cleavable peptide selected from:

SEQ. ID. NO: 185: R-γ-E-P-Orn-G-Hof-E-L-;

SEQ. ID. NO: 186: R-γ-E-P-L-G-(O-benzyl-S)-Y-L-;

SEQ. ID. NO: 187: R - γ -E -P-L-G-(O-benzyl-S)-Y-Nle-;
 SEQ. ID. NO: 188: R -P-L-G-(O-benzyl-S)-Y-L-;
 SEQ. ID. NO: 189: R -P-L-G-(O-methyl-S)-Y-L-;
 SEQ. ID. NO: 190: R -P-L-G-(azaHof)-Y-L-;
 SEQ. ID. NO: 191: R -P-L-G-Hof-Y-L-;
 SEQ. ID. NO: 192: R -P-L-G-Hof-E-L-;
 SEQ. ID. NO: 193: R -P-L-G-(O-benzyl-S)-Y-Nle-;
 SEQ. ID. NO: 194: R -P-L-G-(O-methyl-S)-Y- Nle -;
 SEQ. ID. NO: 195: R -P-L-G-(azaHof)-Y- Nle -;
 SEQ. ID. NO: 196: R -P-L-G-Hof-Y- Nle -;
 SEQ. ID. NO: 197: R -P-L-G-Hof-E- Nle -;
 SEQ. ID. NO: 198: R -P-L-G-(O-benzyl-S)-Y-Hol-;
 SEQ. ID. NO: 199: R -P-L-G-(O-methyl-S)-Y- Hol -;
 SEQ. ID. NO: 200: R -P-L-G-(azaHof)-Y- Hol -;
 SEQ. ID. NO: 201: R -P-L-G-Hof-Y- Hol -;
 and
 SEQ. ID. NO: 202: R -P-L-G-Hof-E- Hol -;

R is selected from: $\text{H}_3\text{CC}(=\text{O})$ -;
 $\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{C}(=\text{O})$ -;
 $\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})$ -;
 $\text{HOC}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})$ -;
 $\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})$ -;
 $\text{H}_3\text{COCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{C}(=\text{O})$ -; and
 tetrazoleacetyl.

10 33. The compound of Claim 1 selected from:

SEQ.ID.NO: 1: 4-methoxy-benzenesulfonyl- β -Ala-G-Hof-Y-L-Dox;
 SEQ.ID.NO: 2: 1,2- C_6H_4 (CO) $_2$ -H-G-Hof-Y-L-Dox;
 SEQ.ID.NO: 3: acetyl -P-L-G-L-L-Dox;
 SEQ.ID.NO: 4: acetyl -P-(R)L-G-L-L-Dox;
 SEQ.ID.NO: 5: acetyl -P -(β -Ala) -G-L-L-Dox;

SEQ.ID.NO: 6:	acetyl -P -(γ-Abu) -G-L-L-Dox;
SEQ.ID.NO: 7:	acetyl -P-Cha-G-L-L-Dox;
SEQ.ID.NO: 8:	P-L-G-L-L-Dox;
SEQ.ID.NO: 9:	MeOCH ₂ CH ₂ OCH ₂ C(=O)- P-L-G-L-L-Dox;
SEQ.ID.NO: 10:	MeOCH ₂ CH ₂ OCH ₂ CH ₂ OCH ₂ C(=O)- P-L-G-L-L-Dox;
SEQ.ID.NO: 11:	H ₂ NCH ₂ CH ₂ N(CH ₂ CH ₂) ₂ NCH ₂ C(=O)- P-L-G-L-L-Dox;
SEQ.ID.NO: 12:	AcHNCH ₂ CH ₂ N(CH ₂ CH ₂) ₂ NCH ₂ C(=O)- P-L-G-L-L-Dox;
SEQ.ID.NO: 13:	AcN(CH ₂ CH ₂) ₂ NCH ₂ C(=O)- P-L-G-L-L-Dox;
SEQ.ID.NO: 17:	Dmg- P-R-Sar-Hof-L-Dox;
SEQ.ID.NO: 18:	acetyl-P-H-G-Hof-L-Dox;
SEQ.ID.NO: 19:	acetyl-P-Orn-G-Hof-L-Dox;
SEQ.ID.NO: 20:	acetyl-P-Dap-G-Hof-L-Dox;
SEQ.ID.NO: 21:	acetyl-P-Cit-G-Hof-L-Dox;
SEQ.ID.NO: 22:	acetyl-P-L-G-(O-(3-pyridyl-))Y-L-Dox;
SEQ.ID.NO: 23:	acetyl-P-L-G-(O-(4-pyridyl-))Y-L-Dox;
SEQ.ID.NO: 24:	acetyl-P-L-G-(4-aza-)Hof-L-Dox;
SEQ.ID.NO: 25:	acetyl-P-L-G-(O-benzyl-)S-L-Dox;
SEQ.ID.NO: 26:	Cbz-P-L-G-(O-(4-pyridylmethyl-))Y-L-Dox;
SEQ.ID.NO: 27:	acetyl -P-L-Sar-L-L-Dox;
SEQ.ID.NO: 28:	acetyl -P- (N-Me-)L-G-L-L-Dox;
SEQ.ID.NO: 29:	acetyl -P- L-G-(N-Me-)L-L-Dox;
SEQ.ID.NO: 30:	acetyl -Hyp- L-G-L-L-Dox;
SEQ.ID.NO: 31:	acetyl -Tzc- L-G-L-L-Dox;
SEQ.ID.NO: 32:	acetyl -(Homo-P)-L-G-L-L-Dox;
SEQ.ID.NO: 33:	acetyl -(Homo-P)-L-G- Hof -L-Dox;
SEQ.ID.NO: 34:	acetyl -(Homo-P)-Orn-G- Hof -L-Dox;
SEQ.ID.NO: 35:	acetyl -Nipecotate -L-G-L-L-Dox;
SEQ.ID.NO: 36:	acetyl -Aze-L-G-L-L-Dox;
SEQ.ID.NO: 37:	acetyl -Chg -L-G-L-L-Dox;
SEQ.ID.NO: 38:	acetyl -P-valerolactam -G-L-L-Dox;
SEQ.ID.NO: 41:	acetyl -L-G-L-Y-L-Dox;
SEQ.ID.NO: 42:	cyclopropylcarbonyl -L-G-L-Y-L-Dox;
SEQ.ID.NO: 43:	cyclobutylcarbonyl -L-G-L-Y-L-Dox;
SEQ.ID.NO: 44:	pivaloyl -L-G-L-Y-L-Dox.
SEQ.ID.NO: 45:	Hyp-G-P-L-G-L-L-Dox;
SEQ.ID.NO: 46:	acetyl -P-L-G-L-A-L-Dox;
SEQ.ID.NO: 47:	acetyl -P-L-G-L-Y-L-Dox;
SEQ.ID.NO: 48:	Peg -P-L-G-L-Y-L-Dox;
SEQ.ID.NO: 49:	H ₃ CC(=O)NH-Peg -P-L-G-L-Y-L-Dox;
SEQ.ID.NO: 50:	AcHNCH ₂ CH ₂ N(CH ₂ CH ₂) ₂ NCH ₂ C(=O)- P-L-G-L-Y-L-Dox;
SEQ.ID.NO: 51:	acetyl -P-L-G-L-S-L-Dox;
SEQ.ID.NO: 52:	acetyl-G-P-L-G-L-L-Dox;
SEQ.ID.NO: 53:	O(CH ₂ CH ₂)NCH ₂ CH ₂ NHC(=O)-G-P-L-G-L-L-Dox;
SEQ.ID.NO: 55:	acetyl -P-L-G-L-L-L-Dox;
SEQ.ID.NO: 58:	Cbz-G-P-L-G-L-L-Dox;
SEQ.ID.NO: 59:	AcHNCH ₂ CH ₂ N(CH ₂ CH ₂) ₂ NCH ₂ C(=O)-G-P-L-G-L-L-Dox;
SEQ.ID.NO: 60:	H ₂ NCH ₂ CH ₂ N(CH ₂ CH ₂) ₂ NCH ₂ C(=O)-G-P-L-G-L-L-Dox;
SEQ.ID.NO: 61:	Dmg-P-L-G-L-L-Dox;

SEQ.ID.NO: 62:	acetyl- γ -E -P-L-G-L-L-Dox;
SEQ.ID.NO: 65:	methoxyacetyl-G-P-L-G-L-L-Dox;
SEQ.ID.NO: 66:	Dmg-P-L-G-Tha-L-Dox;
SEQ.ID.NO: 67:	Dmg-P-L-G-Phg-L-Dox;
SEQ.ID.NO: 68:	Dmg-P-L-G-(O-benzyl-Y)-L-Dox;
SEQ.ID.NO: 69:	Dmg-P-L-G-Bip-L-Dox;
SEQ.ID.NO: 77:	acetyl-G-P-Q-G-L-L-Dox;
SEQ.ID.NO: 78:	acetyl-G-P-R-G-L-L-Dox;
SEQ.ID.NO: 82:	acetyl-G-P-L-G-V-L-Dox;
SEQ.ID.NO: 83:	acetyl-G-P-L-G-Hof-L-Dox;
SEQ.ID.NO: 84:	acetyl-G-P-L-A-L-L-Dox;
SEQ.ID.NO: 85:	Dmg-P-I-G-Bip-L-Dox;
SEQ.ID.NO: 86:	Dmg-P-Chg-G-Bip-L-Dox;
SEQ.ID.NO: 87:	acetyl-G-P-V-G-L-L-Dox;
SEQ.ID.NO: 88:	Dmg-P-I-G-L-L-Dox;
SEQ.ID.NO: 89:	Dmg-P-R-G-Bip-L-Dox;
SEQ.ID.NO: 91:	acetyl-G-P-L-G-E-L-Dox;
SEQ.ID.NO: 92:	Dmg-P-K-G-Bip-L-Dox;
SEQ.ID.NO: 95:	Dmg -P-R-Sar-Hof-R-L-Dox;
SEQ.ID.NO: 96:	Dmg -P-R-G-Hof-R-L-Dox;
SEQ.ID.NO: 97:	Dmg -P-R-G-Bip-R-L-Dox;
SEQ.ID.NO: 98:	acetyl-G-P-L-G-N-L-Dox;
SEQ.ID.NO: 99:	acetyl-G-P-L-G-S-L-Dox;
SEQ.ID.NO: 100:	acetyl-G-P-L-G-(4-hydroxy-phenyl-G)-L-Dox;
SEQ.ID.NO: 101:	acetyl -P-L-G-Hof-H-L-Dox;
SEQ.ID.NO: 102:	acetyl -P-L-G-Hof-A-L-Dox;
SEQ.ID.NO: 103:	acetyl -P-L-G-Hof-Y-L-Dox;
SEQ.ID.NO: 104:	acetyl -P-L-G-Hof- (morpholinylpropyl-G) -L-Dox;
SEQ.ID.NO: 105:	acetyl - γ -E -P-L-G-Hof-Y-L-Dox;
SEQ.ID.NO: 106:	succinyl -P-L-G-Hof-Y-L-Dox;
SEQ.ID.NO: 107:	acetyl -P-L-G-Hof- (O-(4-pyridylmethyl)-Y)-L-Dox;
SEQ.ID.NO: 108:	acetyl -P-L-G-(homo-Y)-Y-L-Dox;
SEQ.ID.NO: 109:	acetyl -P-L-G-(4-aza-Hof)-Y-L-Dox;
SEQ.ID.NO: 110:	acetyl -P-L-G-(O-(4-pyridyl)-Y)-Y-L-Dox;
SEQ.ID.NO: 111:	acetyl -P-L-G-(phenylpropyl-G) -Y-L-Dox;
SEQ.ID.NO: 112:	acetyl -P-L-G-(styryl-A)-Y-L-Dox;
SEQ.ID.NO: 113:	acetyl -P-L-G-(O-benzyl-S)-Y-L-Dox;
SEQ.ID.NO: 114:	acetyl -P- (N,N-dimethyl-K)-G-Hof-Y-L-Dox;
SEQ.ID.NO: 115:	acetyl -P-L-G-Hof-Dap-L-Dox;
SEQ.ID.NO: 116:	acetyl -P-L-G-Hof-Orn-L-Dox;
SEQ.ID.NO: 117:	Peg -P-L-G-Hof-Orn-L-Dox;
SEQ.ID.NO: 118:	acetyl - γ -E -P-L-G-Hof-Orn-L-Dox;
SEQ.ID.NO: 119:	γ -E -P-L-G-Hof-Orn-L-Dox;
SEQ.ID.NO: 120:	acetyl -P-Orn-G-Hof-Orn-L-Dox;
SEQ.ID.NO: 121:	acetyl -P-Orn-G-Hof-Y-L-Dox;
SEQ.ID.NO: 122:	acetyl - γ -E -P-Orn-G-Hof-E-L-Dox;
SEQ.ID.NO: 123:	acetyl -P-Orn-G-L-Y-L-Dox;
SEQ.ID.NO: 124:	acetyl -P-(4-aza-F)-G-L-Y-L-Dox;

SEQ.ID.NO: 125: acetyl -P-L-G-Hof-Dab-L-Dox;
 SEQ.ID.NO: 126: acetyl -P-L-G-Hof-K-L-Dox;
 SEQ.ID.NO: 127: acetyl -P-L-G-Hof- (N,N-dimethyl-K)-L-Dox;
 SEQ.ID.NO: 128: Dmg -P-L-G-Hof-(N,N-dimethyl-K)-L-Dox;
 SEQ.ID.NO: 129: Peg -P-L-G-Hof- (N,N-dimethyl-K)-L-Dox;
 SEQ.ID.NO: 130: acetyl - γ -E -P-L-G-Hof-(N,N-dimethyl-K)-L-Dox;
 SEQ.ID.NO: 131: γ -E -P-L-G-Hof-(N,N-dimethyl-K)-L-Dox;
 SEQ.ID.NO: 132: acetyl -P-L-G-Hof- (N,N-dimethyl-K)-Nle-Dox;
 SEQ.ID.NO: 133: acetyl -P-L-G-Hof- (N,N-dimethyl-K)-Cha-Dox;
 SEQ.ID.NO: 134: acetyl -P-L-G-Hof-Cit-L-Dox;
 SEQ.ID.NO: 135: acetyl - γ -E -P-L-G-Hof-Cit-L-Dox;
 SEQ.ID.NO: 136: acetyl -P-L-G-Hof-Q-L-Dox;
 SEQ.ID.NO: 137: acetyl -P-L-G-Hof-(4-aza-F)-L-Dox;
 SEQ.ID.NO: 138: acetyl -P-L-G-Hof-V-L-Dox;
 SEQ.ID.NO: 139: acetyl - γ -E -P-L-G-Hof-E-L-Dox;
 SEQ.ID.NO: 140: acetyl-G-Aze-L-G-L-L-Dox;
 SEQ.ID.NO: 141: acetyl -(4-fluoro-F)- L-G-L-L-Dox;
 SEQ.ID.NO: 142: acetyl -(homo-P)-L-G-L-Y-L-Dox;
 SEQ.ID.NO: 143: acetyl -(homo-P)-L-G-Hof-Orn-L-Dox;
 SEQ.ID.NO: 144: acetyl -Aze-L-G-L-Y-L-Dox;
 SEQ.ID.NO: 145: acetyl -Aze-L-G-Hof-Orn-L-Dox;
 SEQ.ID.NO: 154: acetyl -P-L-G-L-L-A-L-Dox;
 SEQ.ID.NO: 155: acetyl -P-L-G-L-Y-A-L-Dox;
 SEQ.ID.NO: 156: acetyl -G -P-L-G-L-A-L-Dox;
 SEQ.ID.NO: 157: acetyl -P-L-G-L-A-A-L-Dox;
 SEQ.ID.NO: 158: acetyl -P-L-G-L-A-L-L-Dox;
 SEQ.ID.NO: 159: acetyl -P-L-G-L-L-S-L-Dox;
 SEQ.ID.NO: 160: acetyl -P-L-G-L-L-L-L-Dox;
 SEQ.ID.NO: 161: Dmg -P-L-G-L-Y-L-Dox;
 SEQ.ID.NO: 162: Dmg -P-R-G-Phg-Y-L-Dox;
 SEQ.ID.NO: 163: acetyl -G -P-L-G-L-R-L-Dox;
 SEQ.ID.NO: 164: 4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl -G-Hof-Y-L-Dox;
 SEQ.ID.NO: 165: acetyl -P-L-G-Hof-(N-methylpiperazinepropyl-G)-L-Dox;
 SEQ.ID.NO: 166: tetrazoleacetyl -P-L-G-Hof-Y-L-Dox;
 SEQ.ID.NO: 167: tetrazoleacetyl -P-L-G-(O-benzyl-S)-Y-L-Dox;
 SEQ.ID.NO: 168: tetrazoleacetyl -P-L-G-Hof-Y-Nle-Dox;
 SEQ.ID.NO: 169: P-L-G-(O-benzyl-S)-Y-L-Dox;
 SEQ.ID.NO: 170: acetyl -P-L-G-Hof-(homoY)-L-Dox;
 SEQ.ID.NO: 171: acetyl -P-AzaHof-G-AzaHof-Y-L-Dox;
 SEQ.ID.NO: 172: acetyl -P-L-G-(O-allyl-S)-Y-L-Dox;
 SEQ.ID.NO: 173: acetyl -P-L-G-(4-nitro-Hof)-Y-L-Dox;
 SEQ.ID.NO: 174: acetyl -P-L-G-Hof-AzaHof-L-Dox;
 SEQ.ID.NO: 175: acetyl -P-L-G-(O-methyl-S)-Y-L-Dox;
 SEQ.ID.NO: 176: acetyl - γ -E -P-L-G-(O-benzyl-S)-Y-L-Dox;
 SEQ.ID.NO: 177: acetyl - γ -E -P-L-G-(O-benzyl-S)-Y-Nle-Dox;
 SEQ.ID.NO: 178: 3-pyridinecarbonyl -P-L-G-Hof-Y-L-Dox;
 SEQ.ID.NO: 179: 2-pyrazinecarbonyl -P-L-G-Hof-Y-L-Dox;

SEQ.ID.NO: 180:	acetyl -P-L-G-Hof- (N,N-dimethyl-K)-Nle-Dox;
SEQ.ID.NO: 182:	acetyl -P-L-G-Hof-Y-Hol-Dox;
SEQ.ID.NO: 183:	acetyl -P-L-G-Thr(O-Benzyl)-Y-L-Dox;
SEQ.ID.NO: 184:	acetyl - γ E -P-L-G-Hof-Y-Nle-Dox;

34. The compound of Claim 1 selected from:

SEQ.ID.NO: 39:	acetyl -G-P-L-G-L-F-Dox;
SEQ.ID.NO: 40:	acetyl -G-P-L-G-F-F-Dox;
SEQ.ID.NO: 54:	acetyl-G-P-L-G-L-Y-Dox;
SEQ.ID.NO: 56:	acetyl-G-P-L-G-Bip-F-Dox;
SEQ.ID.NO: 57:	acetyl-G-P-L-G-Nle-F-Dox;
SEQ.ID.NO: 63:	acetyl-G-P-L-G-Tha-F-Dox;
SEQ.ID.NO: 64:	acetyl-G-P-L-G-Phg-F-Dox;
SEQ.ID.NO: 70:	acetyl-G-P-L-G-F-Bip-Dox;
SEQ.ID.NO: 71:	acetyl-G-P-L-G-L-Bip-Dox;
SEQ.ID.NO: 72:	acetyl-G-P-L-G-(2Nal)-Bip-Dox;
SEQ.ID.NO: 73:	acetyl-G-P-L-G-F-A-Dox;
SEQ.ID.NO: 74:	acetyl-G-P-L-G-Bip-A-Dox;
SEQ.ID.NO: 75:	acetyl-G-P-L-G-L-A-Dox;
SEQ.ID.NO: 76:	acetyl-G-P-L-G-(O-benzyl-Y)-F-Dox;
SEQ.ID.NO: 79:	acetyl-G-P-L-G-L-(4-pyridyl-A)-Dox;
SEQ.ID.NO: 80:	acetyl-G-P-L-G-L-R-Dox;
SEQ.ID.NO: 81:	acetyl-G-P-L-G-L-W-Dox;
SEQ.ID.NO: 90:	acetyl-G-P-L-G-L-(O-benzyl-Y)-Dox;
SEQ.ID.NO: 93:	acetyl-G-P-L-G-L-E-Dox;
SEQ.ID.NO: 94:	acetyl-G-P-L-G-Bip-E-Dox;
SEQ.ID.NO: 146:	acetyl -P-L-G-L-Y-G-Dox;
SEQ.ID.NO: 147:	acetyl -P-L-G-Hof-Y-G-Dox;
SEQ.ID.NO: 148:	acetyl -P-L-G-L-Y-(β -homo-L)-Dox;
SEQ.ID.NO: 149:	acetyl -P-L-G-Hof-Y-(β -homo-L)-Dox;
SEQ.ID.NO: 150:	acetyl -P-L-G-L-Y- (β -Ala)-Dox;
SEQ.ID.NO: 151:	acetyl -P-L-G-L-Y-Ahx -Dox;
SEQ.ID.NO: 152:	acetyl -P-L-G-L-Y-Aph -Dox;
SEQ.ID.NO: 153:	acetyl -P-L-G-L-Y-Amh -Dox;
SEQ.ID.NO: 181:	acetyl -P-L-G-Hof-Y-Hos-Dox;

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35. A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.

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36. A method of treating a mammal afflicted with a cancer comprising administering to a mammal afflicted with a cancer a therapeutically effective amount of a compound of Claim 1.

5 37. The method of Claim 36, wherein the cancer is a breast, ovarian, brain, stomach, lung, colon, prostate or liver cancer or wherein the cancer is a leukemia, lymphoma, carcinoma, sarcoma, or melanoma.

10 38. A method of delivering a compound to the cells of a mammal afflicted with a cancer comprising contacting the cells of a mammal afflicted with a cancer with a compound of Claim 1, wherein the contacting is in the presence of a peptidase comprising a matrixin.

15 39. The method of Claim 38, wherein the cancer is a breast, ovarian, brain, stomach, lung, colon, prostate or liver cancer or wherein the cancer is a leukemia, lymphoma, carcinoma, sarcoma, or melanoma.